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CONCLUSIONS: CLO/BU is a mid-intensity allo HSCT regimen with promising anti-leukemic efficacy that seems to be well tolerated without significant cardiac, renal or pulmonary toxicities. CLO/BU resulted in full engraftment by day 30 in all patients. Enrolment is closed; data collection/analysis is ongoing to determine the practicality of this regimen being studied in a multicenter comparative clinical trial.

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MYELOABLATIVE CONDITIONING WITH INTRAVENOUS BUSULPHAN IN A SINGLE DAILY DOSE AND FLUDARABINE (BUF) FOR HLA-IDENTICAL SIBLING ALLOGENEIC HSCT IN MYELOID MALIGNANCIES

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Background: There is a need to improve the conditioning regimens for allogeneic HSCT, reducing the regimen related toxicity while maintaining the anti-leukemic effect. The combination of myeloablative doses of intravenous busulphan (BU) with fludarabine (F) has been utilized with an improved safety profile.
Objective: We aimed to test the efficacy and safety of this combination (BUF), with a single daily dose of BU, since prior pharmacologic and clinical studies support its safety compared with standard 4-daily doses.
Patients: Sixty seven consecutive adult patients undergoing HLA identical sibling allogeneic HSCT for myeloid malignancies were recruited from eight Spanish institutions. Their main characteristics are shown in table 1.

Table 1. Patients characteristics

PATIENTS	67
Age: median (range) years	45 (17-74)
Patients aged > 55 years	30%
Male gender	58%
DISEASE	
AML	35 (52.2%)
MDS Intermediate/High risk	21 (31.3%)
Secondary AML	5 (7.5%)
Myeloproliferative disorder	6 (9%)

Conditioning regimen consisted in BU, one daily IV infusion (3.2 mg/kg/d) for 4 days (total dose 12.8 mg/kg), combined with F, 40 mg/m2 daily (total dose 160 mg/m2). GVHD prophylaxis consisted in cyclosporine and methotrexate. Antimicrobial and other supportive measures were followed at each institution policies. Donor graft source was PB in 76% and BM in 24% of cases. Median CD34 cells infused were 4.0 mill/kg (0.6-17).
Results: All but one patient engrafted, with a median of 14 days (8-34) for 0.5 granulocytes and 12 days (7-46) for 20 platelets. Main toxicities (Bearman) were grade 1. Major toxicity was mucositis (Grade 2 or 3, 38% of cases). There were 3 grade-2 VOD cases (4.5%) which resolved. Acute GVHD grade 2-4 incidence was 22%. Day-100 accumulated mortality was 4.5%. The median follow-up of this ongoing study is 14 months (3-51). At the time of this interim analysis, the relapse free survival is 79.8% and overall survival 80.7%. Major causes of death were relapse (59%) and infection or toxicity (35%).

In conclusion, in the HLA identical allogeneic HSCT setting BUF provides excellent tumour control and low transplant related toxicity and mortality. In particular, the incidence of VOD is < 5%.

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IMPACT OF INJECTION VOLUME AND INFUSION RATE IN A LARGE ANIMAL MODEL DESIGNED TO OPTIMIZE INTRABONE TRANSPLANTATION OF HEMATOPOIETIC STEM CELLS

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Background: The intrabone (IB) route of stem cell administration results in improved engraftment in murine models of transplantation. However, human clinical trials have yet to establish that hematopoietic stem cell (HSC) engraftment is improved with the use of IB delivery. The use of IB vascular access can rapidly restore systemic blood volume and pressure in shock situations, although this access route can be associated with pulmonary emboli. Furthermore, both pressure and shear stress, which have not been characterized with conventional IB delivery techniques, may damage HSCs compromising their ability to engraft. Murine models do not have comparative anatomy or physiology to predict the dynamics of HSC delivery in humans following IB injection. In contrast, swine have similar cardiovascular physiology and size analogous to humans and can be used as a model to study the fluid dynamics of IB injection.
Methods: Forty-five to 60 kg domestic swine were placed under general anesthesia with IB access of the pelvis achieved using an On-Control driver (Vidacare). Isovue was injected into the pelvis at varying volumes and rates and the entire pelvis was imaged by 320-slice ultrafast continuous dynamic CT (Toshiba Aquilion). Pulmonary artery, carotid artery and intramarrow cavity pressures were monitored continuously both during and after injection into the pelvis.
Results: We first characterized the comparative vascular anatomy of the porcine pelvis. The major arterial blood supply to the pelvic bone marrow was found to arise from branches of the internal iliac artery with venous drainage occurring through the iliac vein. IB injection of contrast led to an immediate systemic delivery into the central venous circulation. Reducing the infusion volume and slowing the rate of the infusion both produced smaller increases in IB marrow pressure and post-injection peak pulmonary artery systolic pressure (PASP).

Table 1. Post IB Injection Changes in Intramarrow pressure and Peak PASP

Volume Injected (mL)	Rate Injected (mL/s)	Number of Infusions	Δ Intramarrow Pressure (mmHg) Mean ± S.E.	Δ Peak Pulmonary Artery Systolic Pressure (PASP) (mmHg) Mean ± S.E.
10	0.1	4	159.3 ± 57.7	1.5 ± 0.7
10	0.2	3	300.3 ± 149.3	3.5 ± 1.0
10	0.5	2	803.4 ± 483.0	13.0 ± 5.1
10	1.0	2	1196.0 ± 265.5	8.9 ± 9.3
10	2.5	3	1689.0 ± 116.0	2.2 ± 1.0
5	0.1	2	128.7 ± 60.2	-0.5 ± 0.4
5	0.2	2	256.7 ± 42.7	1.3 ± 1.3
5	0.5	1	802.9	6.1
5	1.0	1	1490.8	0
5	2.5	1	997.5	2

Conclusions: The IB route of injection provides rapid access to the central venous circulation. Increasing IB infusion volumes and/or IB infusion rates led to profound increases in intramarrow pressures and significantly increases PASP. These data suggest continuous monitoring of IB pressures is necessary for studies aimed at characterizing stem cell trafficking and to optimize the retention of HSC in the intrabone marrow space following IB injection.

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VARICELLA ZOSTER REACTIVATION AFTER CORD BLOOD TRANSPLANTATION: COMPARISON WITH UNRELATED BONE MARROW TRANSPLANTATION

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Varicella zoster virus (VZV) infection remains an important problem after allogeneic hematopoietic stem cell transplantation, because VZV-related complications including post-herpetic neuralgia